MJK-008, identified above as the top anti-inflammatory compounds, did not have any effect. Additional examination of MJK-004 effectiveness on bladder cancer cell growth revealed, low IC50 values in BC3C (5.847 uM), EJ28 (6.623 uM) and 5637 (7.582 uM) bladder cancer cell lines relative to MJK-006 (36.37 uM, 352.3 uM, 1738 uM respectively). In addition, MJK-004 reduced significantly, the ability of RT-112 bladder cancer cells to form colonies in soft agar (FIG. **9**). Taken together, these data surprisingly revealed the high efficacy of MJK-004 to suppress bladder cancer cell growth.

TABLE 4

The Efficacy of Suppressing Bladder Cancer Cell Growth

Cancer Cell	IC50 (uM) values			
Line	MJK001	MJK004	MJK006	MJK008
RT-112	9.152	2.374	38.28	ns
UMUC9	7.099	3.971	19.77	ns

MJK-004 targets HDAC4 isoform: To identify MJK-004 HDAC isoform activity, HDAC4 and HDAC9 fluorogenic activity assays were performed. Interestingly, MJK-004 showed high specificity for HDAC4 and very low activity against HDAC9 (FIG. **10**), which is totally opposite regarding the MJK-006 and MJK-008 specificity for HDAC9 (FIG. **7**).

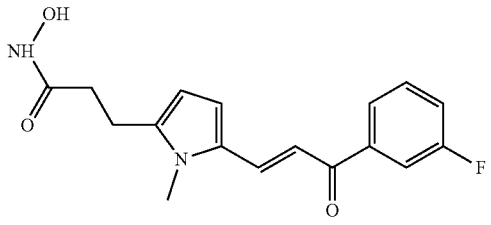
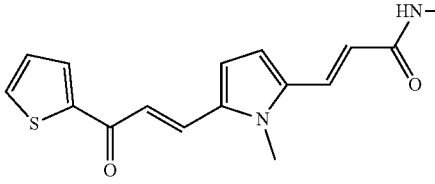
MJK-004 molecular signature in bladder cancer: To examine the genes and signaling pathways affected by MJK-004 treatment in bladder cancer, RNA-sequencing analysis was performed in RT-112 and UMUC9 cell lines. Gene network analysis based on the differentially expressed genes revealed ERK, NURP1 and VEGF as central regulators of MJK-004 effects in RT-112 cells. Similar analysis showed that GPCR, IFN, S100A8, FOXA2, PPARGC1 and IL1 are central regulators of the networks regulated by MJK-004 in UMUC9 bladder cancer cells. Overall, these findings suggest that MJK-004 regulates kinase and metabolic signaling pathways in bladder cancer cells.

MJK-004 and chemotherapy have synergistic effects on bladder cancer: The effects of MJK-004 treatment as a monotherapy or in combination with gemcitabine chemotherapy were evaluated. RT-112 and UMUC9 bladder cancer cells were treated with MJK-004 and/or gemcitabine (10 nM—low concentration) and cell growth was evaluated on days 4 & 5 (FIG. **11**). Interestingly, MJK-004 suppressed bladder cancer growth in both cell lines as a monotherapy. MJK-004 combination with gemcitabine increased gemcitabine's efficacy in RT-112 and UMUC9 bladder cancer cells. These findings suggest that MJK-004 is highly effective to suppress bladder cancer cell growth in combination with low concentration of gemcitabine chemotherapy.

[0237] The synthesized series of MJK chemical compounds have increased specificity for HDAC9 or HDAC4 isoforms. Interestingly, MJK-008 and MJK-006 are highly effective in blocking inflammation in vitro and in vivo through regulation of HDAC9, while they did not have any effect on cancer cell growth. On the other hand, MJK-004 is highly efficient in blocking bladder cancer cell growth through regulation of HDAC4 isoform. MJK-006 and MJK-008 compounds have the potential to be developed as therapeutics for Crohn's Disease and other auto-immune diseases. MJK-004 compound has the potential to developed as a therapeutic against bladder cancer in combination with chemotherapy. The findings for MJK-006, -008 and -004 compounds are shown in Table 5.

TABLE 5

The Activity of MJK-006, -008 and -004 Compounds

Compound	HDAC4	Bladder ca	HDAC9	Crohn's
 MJK004	++	++	++	++
 MJK004	+++	++++	+	+